Bystander Exposure Assessment for the Pesticide 1,3-Dichloropropene

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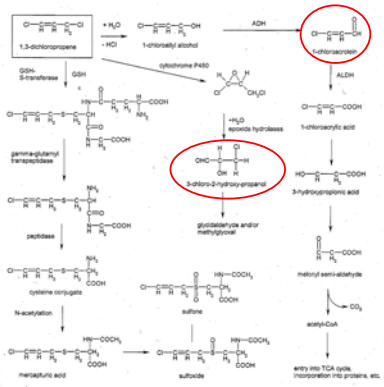
SUMMARY

Telone aka 1,3-Dichloropropene (1,3-D) is a volatile organic compound widely used throughout California as a pre-plant soil fumigant to control all major types of parasitic plant nematodes, centipedes, wire worms and plant diseases associated with these parasites. 1,3-D is classified by the US EPA as B2, a probable human carcinogen. Cancer risk from this pesticide is mitigated in California by regulations requiring township caps and by the use of buffer zones between application areas and bystanders. Using county-specific pesticide use data and meteorological data in conjunction with modeling tools, air concentration estimates were developed for two high use counties in California. Using several scenarios, bystander cancer risk estimates ranged from $0.95x10^{-5}$ to $1.5x10^{-5}$. In addition, data are available for a year of air monitoring in Parlier in Fresno County (the highest use county in California). Using this monitoring data, the cancer risk was estimated to be $3.4x10^{-5}$ which is in excellent agreement with the modeling estimates. Mitigation measures, such as township caps, field tarps, deep shank application, and the addition of soil amendments, may be used to reduce cancer risk.

METABOLISM OF 1,3-DICHLOROPROPENE

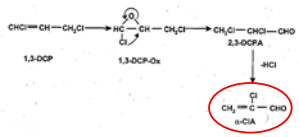
Major pathway: conjugation with glutathione & elimination in urine as mercapturic acid & sulfoxide or sulfone derivatives or by hydrolysis and dechlorination followed by reaction with alcohol dehydrogenase to form mutagenic 1-chloroacrolein (1).

Minor pathway: reaction with P450 to form mutagenic epoxides that convert into the mutagen 3-chloro-2-hydroxy-propanol (1).



AUTO-OXIDATION OF 1,3-DICHLOROPROPENE

Auto-oxidation (during storage or field application) yields the highly mutagenic alpha-chloroacrolein (α-ClA) (2).



EVIDENCE FOR GENOTOXICITY OF 1,3-D & DERIVATIVES

Bacterial test systems: Unpurified 1,3-D is mutagenic in Ames Salmonella tests with & without metabolic activation (2-10), but glutathione (GSH) protects against this activity (6, 9, 10).

Mammalian test systems: 1,3-D triggers unscheduled DNA synthesis in hamster lung V79 cells & rat hepatocytes after GSH depletion (11); sister chromatid exchange in V79 cells (12), Chinese Hamster Ovary (CHO) cells (13), & human lymphocytes in vitro (14).

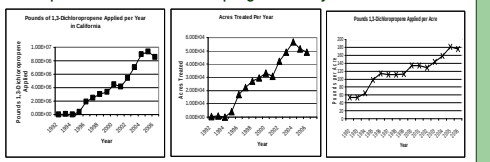
Animal studies: Rodent inhalation studies show morphological alterations in nasal tissues, hyperplasia of urinary bladder lining, and benign lung tumors (15).

Human medical reports: A possible relationship between high 1,3-D exposure & pancreatic or hematologic malignancies is suggested by case reports (16) & by an epidemiological study (17).

Summary: Under field conditions, 1,3-D formulations are likely to contain mutagenic impurities. In addition, some 1,3-D metabolites are mutagenic.

ANNUAL USE OF 1,3-DICHLOROPROPENE IN CALIFORNIA

In 1990, use of 1,3-D was suspended in California after air monitoring stations detected levels of concern in ambient air. In 1995 the suspension was lifted after the adaption of mitigation measures including a township cap of 90,250 adjusted pounds per year per township. In 2002 township caps were increased to 180,250 adj lbs per year for those townships where annual use was under the 90,250 annual cap. Changing regulations, plus phase-out of methyl bromide, have resulted in a large increase in 1,3-D use with more treated acres & higher application rates. These increases may lead to underestimation of health risks because previous estimates were based on older use patterns. Therefore, a new exposure assessment is in progress for bystanders & workers.



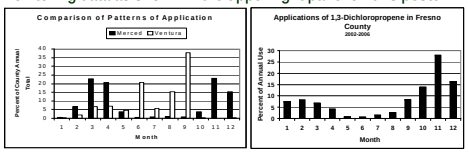
AIR DISPERSION MODELING

1,3-D is applied to soil of up to 40 acres per day by drip or up to 80 acres per day by shallow or deep shank injection. 1,3-D volatilizes and moves downwind in a plume that is affected by wind speed and direction as illustrated by the contour plots shown below. Lifetime bystander exposures were estimated using flux measurements taken after field applications in Merced or Ventura counties and actual weather data from the same areas. Two lifetime exposure scenarios were considered. Low mobility assumes that residents spend their entire lifetime within the highest use township (36 square miles). Intermediate mobility assumes that residents spend their entire lifetime within a 3x3 township area (324 square miles).

MONTHLY USE PATTERNS FOR 1,3-D (2002-2006)

The chart on the lower left compares the monthly use patterns of 1,3-D application in the two high use counties (Merced & Ventua) that were used in the modeling studies. High use months are defined as those in which ≥5% of the annual total is applied. Merced has 5 high use months annually, while Ventura has 6. These show monthly averages for the period 2002-2006.

The chart on the lower right shows the monthly application pattern for Fresno county (ranked #1 in annual 1,3-D use) with 7 high use months annually. Air monitoring data were collected in the town of Parlier which resides in this county. Exposure estimates from the modeling data below are compared to estimates from this air monitoring data as shown in the upper right panel on this poster.



MODELING ESTIMATE OF BYSTANDER LIFETIME EXPOSURE MERCED TOWNSHIP *(Use Rank #3)*

The cancer risk estimates below are based on SOFEA simulations of the cumulative long-term air concentrations based on a level of 180,500 adjusted pounds of 1,3-D per township per year (18). Air concentrations were entered into a simulation model (HEE5CB) along with body weights, breathing rates, and other parameters to produce a frequency distribution of lifetime exposures. Upper bound and lower bound Lifetime Average Daily Doses (LADD) bracket the 95th percentile. The risk estimates shown below were calculated by multiplying the upper or lower bound LADD by the potency factor of $5.5x10^{-5}$ kg-day/ug (19). Low mobility is the most conservative scenario considered.

Bystander	Mobility	Lower Bound Cancer Risk	Upper Bound Cancer Risk
Male	Low	$1.35x10^{-5}$	$1.5x10^{-5}$
Male	Intermediate	$1.17x10^{-5}$	$1.31x10^{-5}$
Female	Low	$1.32x10^{-5}$	$1.46x10^{-5}$
Female	Intermediate	$1.18x10^{-5}$	$1.31x10^{-5}$

MODELING ESTIMATE OF BYSTANDER LIFETIME EXPOSURE VENTURA TOWNSHIP *(Use Rank #7)*

The cancer risk estimates below were calculated as described for Merced (above) except that flux & weather data were from Ventura (18). In addition, the application configuration assumed a use level of 135,375 adjusted lbs/yr for a 5x5 township area plus 21 surrounding townships applying less than 90,250 adjusted lbs/yr.

Bystander	Mobility	Lower Bound Cancer Risk	Upper Bound Cancer Risk
Male	Low	$1.06x10^{-5}$	$1.28x10^{-5}$
Male	Intermediate	$0.95x10^{-5}$	$1.18x10^{-5}$
Female	Low	$1.04x10^{-5}$	$1.26x10^{-5}$
Female	Intermediate	$0.96x10^{-5}$	$1.19x10^{-5}$

AIR MONITORING DATA FROM PARLIER (FRESNO COUNTY) TO ESTIMATE BYSTANDER EXPOSURE

Fresno County is #1 in California in terms of pounds of 1,3-D used per year. The town of Parlier is in this heavily agricultural county. Because of air quality issues, a one year study was done in the town of Parlier in which air was sampled at least once or twice a week at several locations for an entire year. Dr. Jay Schreider (DPR, Medical Toxicology Branch) calculated the chronic air levels of 1,3-D from the one year average of all air sampling days & sites in Parlier. The lifetime cancer risk based on this extensive monitoring data is in excellent agreement with the cancer risk derived from modeling studies based on Merced and Ventura field flux & annual weather data.

Estimation Basis	County	Rank for 1,3-D Use	Cancer Risk Estimate
One Year Air Monitoring Data *(Parlier)*	**Fresno**	**1**	**$3.4x10^{-5}$**
SOFEA Modeling With Merced Field Flux & Weather Data	**Merced**	**3**	**$1.17x10^{-5}$ to $1.5x10^{-5}$**
SOFEA Modeling With Ventura Field Flux & Weather Data	**Ventura**	**7**	**$0.95x10^{-5}$ to $1.28x10^{-5}$**

CONCLUSIONS

1. Telone (1,3-dichloropropene; 1,3-D) plays an important role in agriculture as a pre-plant fumigant.
2. Numerous assays establish 1,3-D and/or its metabolic & auto-oxidation products as genotoxins.
3. Exposure assessments based on modeling field flux data, application patterns, & weather for high use counties suggest a level of concern with respect to cancer risk for lifetime exposure.
4. In-town (Parlier) air monitoring studies with data collected for one year agree with cancer risk estimates based on modeling and confirm the validity of the modeling assumptions.
5. Mitigation measures (i.e., township caps, field tarps, & changes in application methods) may be used to reduce cancer risk.

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